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PATENT
Attorney Docket No. **OPHD-02304**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: James A. Williams *et al.*
Serial No.: 08/704,159 Group No.: 1816
Filed: August 28, 1996 Examiner:
Entitled: **MULTIVALENT VACCINE FOR *CLOSTRIDIUM BOTULINUM* NEUROTOXIN**

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Assistant Commissioner for Patents
Washington, D.C. 20231

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Dated: September 2, 1997 By: Marilyn Moy
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Dated: September 2, 1997

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In re Application of:	James A. Williams *et al.*	
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By: Marilyn Moy
Marilyn Moy

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed patent is referred to in the body of the specification:

- U.S. Patent No. 5,080,895, issued January 14, 1992, to Tokoro;

The following printed publications are referred to in the body of the specification:

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Applicants have become aware of the following printed publications which may be material to the examination of this application:

- East *et al.* (1992) "Sequence of the gene encoding type F neurotoxin of *Clostridium botulinum*," FEMS Micro. Letters 96:225-230. East *et al.* describes the cloning strategy and sequence determination of *Clostridium botulinum* type F toxin gene, and discloses the nucleotide sequence of that gene. However, East *et al.* does not disclose (a) host cells containing a recombinant expression vector which encodes at least a portion of *Clostridium botulinum* type B or type E toxin, (b) host cells which express a fusion protein comprising a non-toxin

portion and at least a portion of *Clostridium botulinum* type B or type E toxin, (c) vaccines comprising such fusion proteins, or (d) methods of generating antibodies using such fusion proteins;

- Niemann (1992) "Clostridial Neurotoxins - Proposal of a Common Nomenclature," Toxicon 30:223-225. Niemann proposes a common nomenclature for the neurotoxins of *Clostridium tetanus* and *Clostridium botulinum*. However, Niemann does not disclose (a) host cells containing a recombinant expression vector which encodes at least a portion of *Clostridium botulinum* type B or type E toxin, (b) host cells which express a fusion protein comprising a non-toxin portion and at least a portion of *Clostridium botulinum* type B or type E toxin, (c) vaccines comprising such fusion proteins, or (d) methods of generating antibodies using such fusion proteins;
- Food and Drug Administration Document (Docket No. 79D-0465) 53 FR 5044, February 19, 1988. The Food and Drug Administration announced in this document the availability of a guideline for the use of the Limulus Amebocyte Lysate (LAL) test as an end-product endotoxin test for human injectable drugs (including biological products), animal injectable drugs, and medical devices. By following the procedures set forth in the guideline, manufacturers of the above mentioned products may use the LAL test as an alternative to the official rabbit pyrogen test. In contrast to the claimed invention, this document does not discuss (a) host cells containing a recombinant expression vector which encodes at least a portion of *Clostridium botulinum* type B or type E toxin, (b) host cells which express a fusion protein comprising a non-toxin portion and at least a portion of *Clostridium botulinum* type B or type E toxin, (c) vaccines comprising such fusion proteins, or (d) methods of generating antibodies using such fusion proteins;
- Food and Drug Administration Document (Docket No. 79D-0465) 48 FR 27835, June 17, 1983. In this document, the Food and Drug Administration decided to extend the comment period for the notice announcing the availability of a draft guideline. The guideline was drafted for validation of the LAL test as an end-product endotoxin test for human and animal parenteral drugs,

biological products, and medical devices. Unlike the claimed invention, this document does not disclose (a) host cells containing a recombinant expression vector which encodes at least a portion of *Clostridium botulinum* type B or type E toxin, (b) host cells which express a fusion protein comprising a non-toxin portion and at least a portion of *Clostridium botulinum* type B or type E toxin, (c) vaccines comprising such fusion proteins, or (d) methods of generating antibodies using such fusion proteins; and

- Food and Drug Administration Document (Docket No. 79D-0465) 48 FR 13096, March 29, 1983. The Food and Drug Administration announced in this document the availability of a draft guideline for use of the LAL test as an end-product endotoxin test for human, biological, and animal injectable drugs and medical devices. However, this document does not disclose (a) host cells containing a recombinant expression vector which encodes at least a portion of *Clostridium botulinum* type B or type E toxin, (b) host cells which express a fusion protein comprising a non-toxin portion and at least a portion of *Clostridium botulinum* type B or type E toxin, (c) vaccines comprising such fusion proteins, or (d) methods of generating antibodies using such fusion proteins.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: September 2, 1997

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